

PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL SEARCHING AUTHORITY

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT AND
THE WRITTEN OPINION OF THE INTERNATIONAL
SEARCHING AUTHORITY, OR THE DECLARATION

To:

GENENCOR INTERNATIONAL, INC.
Attn. Macknight, Kamrin T.
925 Page Mill Road
Palo Alto, California 94304
UNITED STATES OF AMERICA

(PCT Rule 44.1)

Date of mailing
(day/month/year)

05/09/2005

Applicant's or agent's file reference

GC819 - 2 - PCTB

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/US2004/039066

International filing date
(day/month/year)

19/11/2004

Applicant

GENENCOR INTERNATIONAL, INC.

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Stefanie Büchler

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Annexes B1 and B2).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, Volume I/A, paragraph 296).

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference GC819 - 2 - PCTB	FOR FURTHER ACTION <small>see Form PCT/ISA/220 as well as, where applicable, item 5 below.</small>	
International application No. PCT/US2004/039066	International filing date (day/month/year) 19/11/2004	(Earliest) Priority Date (day/month/year) 19/11/2003
Applicant GENENCOR INTERNATIONAL, INC.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box II).

3. ☒ **Unity of invention is lacking** (see Box III).

4. With regard to the title,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

a. the figure of the **drawings** to be published with the abstract is Figure No. 6

☒ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2004/039066

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☐ contained in the international application as filed
 - ☐ filed together with the international application in computer readable form
 - ☒ furnished subsequently to this Authority for the purpose of search
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/039066

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-47, 54-84, 87-98, 103, 105-107, 109 completely; 48-53, 85, 86 partially

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-47,54-84,87-98,103,105-107,109 completely; 48-53,85,86 partially

An isolated serine protease obtained from a member of the Micrococcinea, in particular from Cellulomonas 69B4 according to SEQ ID NO:8, encoding polynucleotides, in particular according to SEQ ID NO:1 and 4, mutants and variants thereof, as well as related subject-matter as claimed. Said variants being in particular serine proteases from other Cellulomonas species according to SEQ ID NO:53-66.

2. claims: 48-53,85,86 partially

idem for SEQ ID NO:67,68 (*Oerskovia turbata*)

3. claims: 48-53,85,86 partially

idem for SEQ ID NO:69,70 (*Oerskovia jenensis*)

4. claims: 48-53,85,86 partially

idem for SEQ ID NO:71,72 (*Cellulosimicrobium cellulans*)

5. claims: 48-53,85,86 partially

idem for SEQ ID NO:73,74 (*Promicromonospora citrea*)

6. claims: 48-53,85,86 partially

idem for SEQ ID NO:75,76 (*Promicromonospora sukumoe*)

7. claims: 48-53,85,86 partially

idem for SEQ ID NO:77,78 (*Xylanibacterium ulmi*)

8. claims: 99-102,104,108 completely

A cleaning composition that comprises at least one stable enzyme, said cleaning composition comprising a sufficient amount of a pH modifier to provide said composition with a neat pH of from about 3 to about 5, said composition being essentially free of materials that hydrolyze at a pH of from about 3 to about 5, as well as subject-matter related thereto.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/039066

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/53 C12N9/64

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BIOSIS, EMBASE, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE NCBI 'Online! 11 August 2003 (2003-08-11), RAOULT D. ET AL.: XP002327070 Database accession no. AA044722	1,2,7, 11,44-47
Y	abstract	89-91, 109
X	SHIMOI HITOSHI ET AL: "Molecular structure of Rarobacter faecitabidus protease I; A yeast-lytic serine protease having mannose-binding activity" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 267, no. 35, 1992, pages 25189-25195, XP002327067 ISSN: 0021-9258	1,2,7,42
Y	the whole document	89-91, 109
	----- -/--	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

6 June 2005

Date of mailing of the international search report

35. 09. 2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040. Tx. 31 651 epo nl.
Fax: (+31-70) 340-3016

Authorized officer

Kania, T

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/039066

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MINE O M ET AL: "USE OF DEGENERATE PRIMERS AND HEAT-SOAKED POLYMERASE CHAIN REACTION(PCR) TO CLONE A SERINE PROTEASE ANTIGEN FROM DERMATOPHILUS CONGOLENSIS" IMMUNOLOGY AND CELL BIOLOGY, CARLTON, AU, vol. 75, no. 5, October 1997 (1997-10), pages 484-491, XP008000691	1,2,7,42
Y	the whole document	70,76, 89-91
X	----- SAEKI KAZUO ET AL: "Purification and characterization of an alkaline protease from Oerskovia xanthineolytica TK-1" JOURNAL OF FERMENTATION AND BIOENGINEERING, vol. 77, no. 5, 1994, pages 554-556, XP002327068 ISSN: 0922-338X	1-3
Y	the whole document	70,71, 76,89-91
X	----- LONGSHAW C M ET AL: "Kytococcus sedentarius, the organism associated with pitted keratolysis, produces two keratin-degrading enzymes." JOURNAL OF APPLIED MICROBIOLOGY, vol. 93, no. 5, 2002, pages 810-816, XP002327069 ISSN: 1364-5072	1,2
Y	the whole document	70,71, 89-91
X	----- WO 01/58276 A (F HOFFMANN-LA ROCHE AG; OESTERGAARD, PETER, RAHBK; SJOEHOLM, CARSTEN) 16 August 2001 (2001-08-16)	8,11
Y	the whole document	109
X	----- DATABASE EMBL 'Online! 20 June 2002 (2002-06-20), HONG S.: XP002327071 retrieved from EBI Database accession no. AF515832	61-64
Y	abstract	65,66, 87-89
Y	----- US 5 646 028 A (LEIGH ET AL) 8 July 1997 (1997-07-08) cited in the application the whole document -----	65,66, 70,71, 76, 87-91, 109

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/039066

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0158276	A	16-08-2001	AU 777210 B2	07-10-2004
			AU 3544601 A	20-08-2001
			AU 781415 B2	19-05-2005
			AU 4236601 A	20-08-2001
			BR 0108164 A	21-01-2003
			BR 0108165 A	25-02-2003
			CA 2395266 A1	16-08-2001
			CA 2395343 A1	16-08-2001
			CN 1398161 A	19-02-2003
			CN 1398162 A	19-02-2003
			WO 0158275 A2	16-08-2001
			WO 0158276 A2	16-08-2001
			EP 1257175 A2	20-11-2002
			EP 1257176 A2	20-11-2002
			JP 2003521907 T	22-07-2003
			JP 2003521908 T	22-07-2003
			MX PA02007613 A	13-12-2002
			MX PA02007614 A	13-12-2002
			PL 357638 A1	26-07-2004
			PL 357668 A1	26-07-2004
			US 2005148060 A1	07-07-2005
			US 2004161448 A1	19-08-2004
			US 2001026797 A1	04-10-2001
			US 2003021774 A1	30-01-2003
US 5646028	A	08-07-1997	NONE	

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2004/039066

International filing date (day/month/year)
19.11.2004

Priority date (day/month/year)
19.11.2003

International Patent Classification (IPC) or both national classification and IPC
C12N15/53, C12N9/64

Applicant
GENENCOR INTERNATIONAL, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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10/576331

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2004/039066

IAP20 RECEIVED 13 APR 2006

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☒ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☒ in written format
☒ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☒ furnished subsequently to this Authority for the purposes of search.
3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43bis.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/039066

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 48-53, 85, 86 partially; 99-102, 104, 108 completely

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. 48-53, 85, 86 partially; 99-102, 104, 108 completely
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/039066

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
- ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☒ not paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-47,54-84,87-98,103,105-107,109 completely; 48-53,85,86 partially

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	4-6,9,10,12-41,43,48-60,65-98,103,105-107,109
	No: Claims	1-3,7,8,11,42,44-47,61-64
Inventive step (IS)	Yes: Claims	1-3,7,8,11,41,43-46,60-63
	No: Claims	65,66,70,71,76,87-91,109
Industrial applicability (IA)	Yes: Claims	1-98,103,105-107,109
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**WRITTEN OPINION OF THE
 INTERNATIONAL SEARCHING
 AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2004/039066

The present written opinion refers to the following documents cited in the search report:

- D1: DATABASE NCBI [Online] 11 August 2003 (2003-08-11), RAOULT D. ET AL.:
 Database accession no. AA044722
- D2: SHIMOI HITOSHI ET AL: "Molecular structure of *Rarobacter faecitabidus* protease I; A yeast-lytic serine protease having mannose-binding activity" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 267, no. 35, 1992, pages 25189-25195, ISSN: 0021-9258
- D3: MINE O M ET AL: "USE OF DEGENERATE PRIMERS AND HEAT-SOAKED POLYMERASE CHAIN REACTION(PCR) TO CLONE A SERINE PROTEASE ANTIGEN FROM DERMATOPHILUS CONGOLENSIS" IMMUNOLOGY AND CELL BIOLOGY, CARLTON, AU, vol. 75, no. 5, October 1997 (1997-10), pages 484-491,
- D4: SAEKI KAZUO ET AL: "Purification and characterization of an alkaline protease from *Oerskovia xanthineolytica* TK-1" JOURNAL OF FERMENTATION AND BIOENGINEERING, vol. 77, no. 5, 1994, pages 554-556, ISSN: 0922-338X
- D5: LONGSHAW C M ET AL: "Kytococcus sedentarius, the organism associated with pitted keratolysis, produces two keratin-degrading enzymes." JOURNAL OF APPLIED MICROBIOLOGY, vol. 93, no. 5, 2002, pages 810-816, ISSN: 1364-5072
- D6: WO 01/58276 A (F HOFFMANN-LA ROCHE AG; OESTERGAARD, PETER, RAHBK; SJOEHOLM, CARSTEN) 16 August 2001 (2001-08-16)
- D7: DATABASE EMBL [Online] 20 June 2002 (2002-06-20), HONG S.: retrieved from EBI Database accession no. AF515832
- D8: US-A-5 646 028 (LEIGH ET AL) 8 July 1997 (1997-07-08)

Subject-matter of the application

The application relates to the cloning and characterization of a serine protease from *Cellulomonas* strain 69B4 as well as the cloning of variants from other members of the *Micrococcineae*. The enzymes are used in cleaning compositions and animal feeds. Further, cleaning compositions characterized by the presence of one acid stable enzyme are claimed.

Re Item IV: Non-unity

1. The present set of claims lacks unity. 8 potential inventions have been recognized (see International Search Report (ISR), Sheet 206).

Rule 13.2 PCT stipulates that where a group of inventions is claimed the requirement of unity shall be fulfilled only where there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. "Special" technical features are those features that define a contribution which each of the inventions makes over the prior art.

The technical features shared by the presently claimed inventions is that the sequences all encode serine proteases from microorganisms from the Micrococcineae. The existence of serine proteases in e.g. Oerskovia was known in the prior art (see D4, D5). Further, serine proteases have been cloned from members of the Micrococcineae in the past (see D1-D3). The common technical features therefore cannot define a contribution over the prior art, and each individual serine protease, its encoding sequences and uses thereof have to be considered an independent potential invention.

Further, the subject-matter of invention 8 relates to a cleaning composition in general. No relation to the present serine proteases is required by the corresponding claims. This subject addresses an entirely different technical problem than the other 7 inventions and consequently is considered an individual potential invention.

2. Due to the fact that Applicant has not elected to pay additional search fees for the other inventions (subjects 2-8, ISR Sheet 206), the following opinion is restricted to the subject-matter of potential invention 1.

Re Item V: Novelty and Inventive step

1. The subject-matter of present claims 4-6, 9, 10, 12-41, 43, 48-60, 65-98, 103, 105-107, 109 has not been disclosed in the prior art and is thus considered as novel.
2. The subject-matter of claims 1-3, 7, 8, 11, 42, 44-47, 61-64 is either disclosed or at least anticipated in cited documents D1-D7 and consequently not novel (**Article 33(2) PCT**).

Serine proteases have been isolated and cloned from members of the Micrococcineae as disclosed in D1-D5.

The serine protease from Nocardiosis disclosed in D6 shows > 60% identity to SEQ

ID NO:8.

The polynucleotide sequence encoding the serine protease disclosed in D7 shows > 70% identity to SEQ ID NO:4.

3. The subject-matter of claims 65, 66, 70, 71, 76, 87-91, 109 is regarded as common knowledge in the art, in particular with regard to cited documents D6 (animal feed) and D8 (cleaning compositions). The said claims are therefore not inventive (**Article 33(3) PCT**).

Re Item VIII: Clarity

1. Claims 1-4, 6, 7, 42-47, 70-72, 75, 76, 89-98, 103, 105-107, 109 lack clarity. The claimed subject-matter is merely defined by functional features and/or desirable characteristics. A product, however, has to be defined by structural features which in the present case means the polynucleotide and polypeptide sequences concerned.
2. Claims 11 and 60 relate to variant serine proteases which are characterized by being different from the serine protease according to SEQ ID NO:8 by the substitution of at least one amino acid.
In the most extreme case, this would mean that every amino acid of the sequence according to SEQ ID NO:8 is substituted, which would lead to a completely different, undefined molecule.

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